

Modeling Approaches to Metabolic (and Other) Pathways

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Some Statistical Approaches

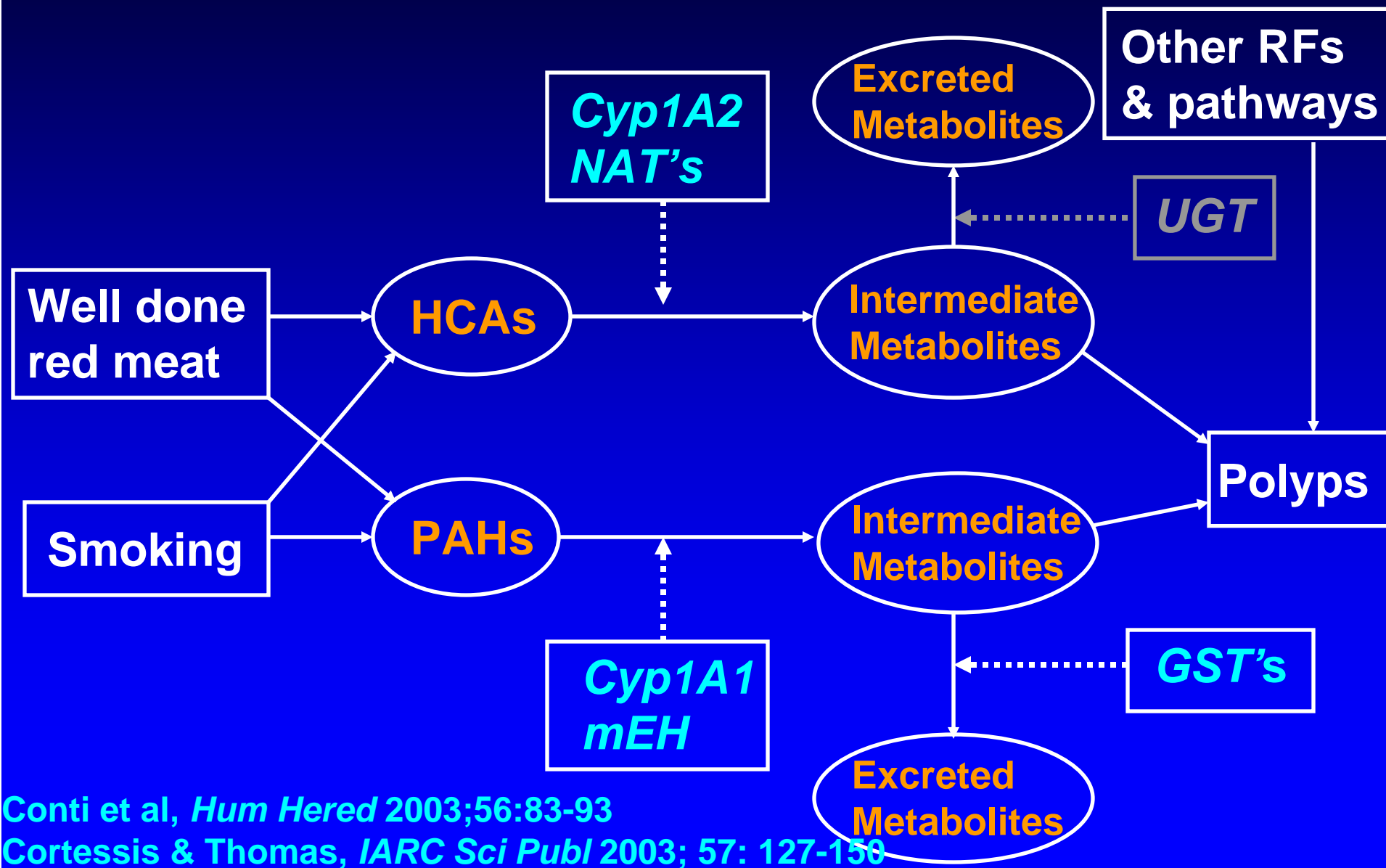
- One-at-a-time and pairwise descriptive analyses
- **Multivariate models (e.g., logistic)**
- Hierarchical models
- Model selection and model averaging
- Exploratory approaches (CART, neural nets, clustering, etc.)
- Mechanistic models (e.g., PBPK)

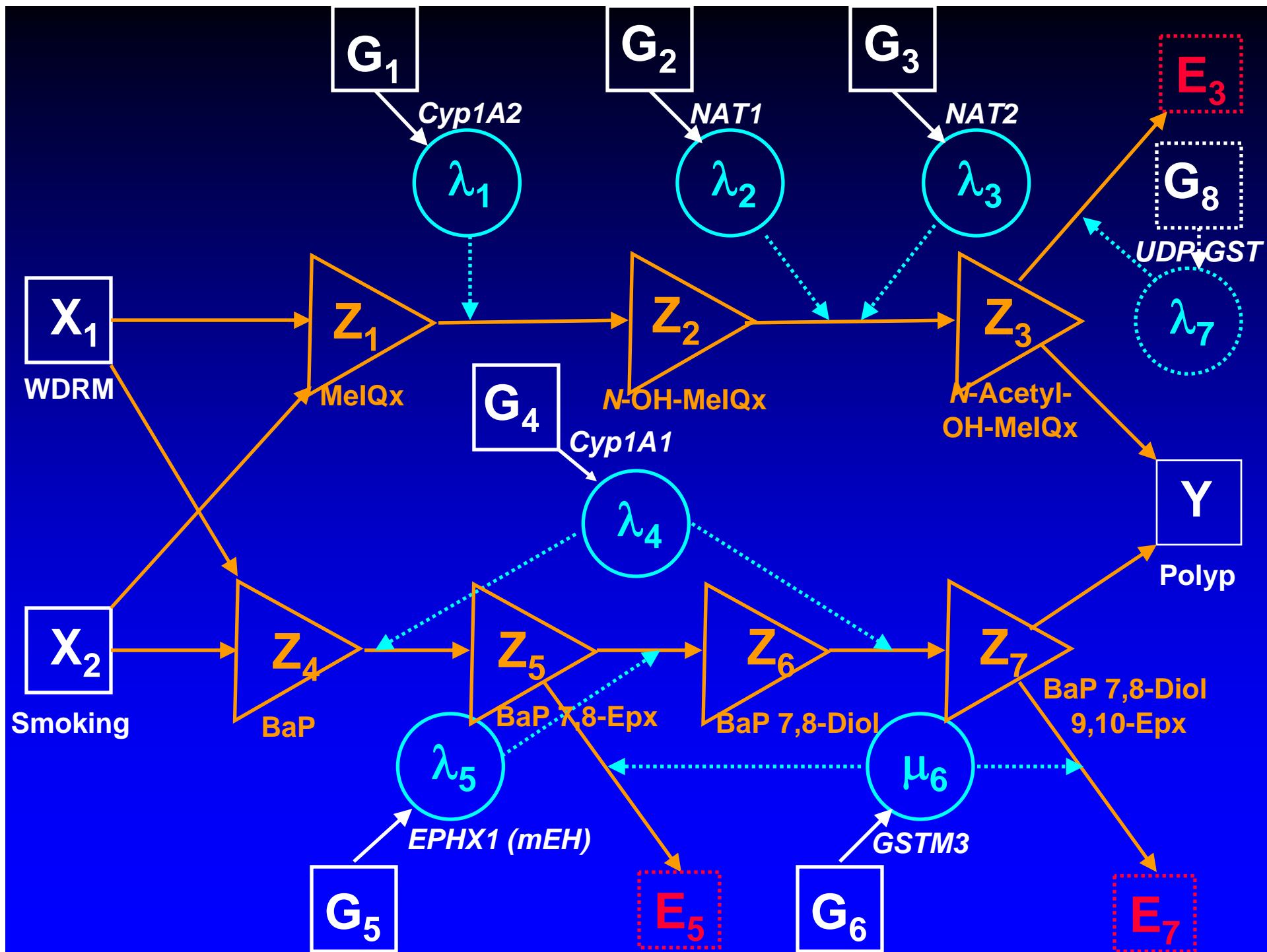
Hierarchical Modeling

- “Empirical” method based on regression modeling of main effects and interactions
- Uses “prior covariates” to inform estimation of effects using pathway concepts and genomic/metabolomic data
- Uses Bayesian model averaging to account for model uncertainty

Conti et al, *Hum Hered* 2003;56:83-93
Hung et al, *CEBP* 2004,13:1013-24

Conceptual Model for HCA & PAH Pathways for Colorectal Polyps





What's Needed to Make Progress

- Biomarkers
 - Exposure
 - Intermediate metabolites
 - Enzyme activity levels
 - DNA adducts, damage, methylation
 - Preclinical markers of disease



